

Amendments to the Specification

Please replace the paragraph appearing at page 13, lines 1-3 with the following amended paragraph:

FIGURE 4C depicts the isolated DNA coding sequence for the *dnaX* gene (also present in FIGURES 4A and 4B 3A and 3B) in accordance with the invention, which corresponds to SEQ. ID. No. 3.

Please replace the paragraph appearing at page 75, lines 7-31 with the following amended paragraph:

The XbaI insert encoded an open reading frame, starting with a GTG codon, of 529 amino acids in length (58.0 kDa), closer to the predicted length of the *B. subtilis* τ subunit (563 amino acids, 62.7 kDa mass)(Alonso et al., 1990) than the *E. coli* τ subunit (71.1 kDa)(Yin et al., 1986). The *dnaX* gene encoding the γ/τ subunits of *E. coli* DNA polymerase III holoenzyme is homologous to the *holB* gene encoding the δ' subunit of the γ complex clamp loader, and this homology extends to all 5 subunits of the eukaryotic RFC clamp loader as well as the bacteriophage gene protein 44 of the gp44/62 clamp loading complex (O'Donnell et al., 1993). These gene products show greatest homology over the N-terminal 166 amino acid residues (of *E. coli dnaX*); the C-terminal regions are more divergent. Fig. 4 shows Figures 5A-B show an alignment of the amino acid sequence of the N-terminal regions of the *T.th. dnaX* gene product to those of several other bacteria. The consensus GXXGXGKT (SEQ. ID. No. 17) motif for nucleotide binding is conserved in all these protein products. Further, the *E. coli* δ' crystal structure reveals one atom of zinc coordinated to four Cys residues (Guenther, 1996). These four Cys residues are conserved in the *E. coli dnaX* gene, and the γ and τ subunits encoded by *E. coli dnaX* bind one atom of zinc. These Cys residues are also conserved in *T.th. dnaX* (shown in Fig. 4 Figures 5A-B). Overall, the level of amino acid identity relative to *E. coli dnaX* in the N-terminal 165 residues of *T.th. dnaX* is 53 %. The *T.th. dnaX* gene is just as homologous to the *B. subtilis dnaX* (53 % identity) gene relative to *E. coli dnaX*. After this region of homology, the C-terminal region of *T.th. dnaX* shares 26% and 20% identity to *E. coli* and *B. subtilis dnaX*, respectively. A proline rich region, downstream of the conserved region, is also present in *T.th. dnaX* (residues 346-375), but not in the *B. subtilis dnaX* (see Figs. 3A and 3B). The overall identity between *E. coli dnaX* and *T.th. dnaX* over the entire gene is 34%. Identity of *T.th. dnaX* to *B. subtilis dnaX* over the entire gene is 28%.

Please replace the paragraph appearing at page 103, lines 15-25 with the following amended paragraph (note that underlining of the sequences appears in the original text):

The *Aquifex aeolicus holB* gene was not previously identified by the genome sequencing facility at Diversa (Deckert et al., 1998). The *Aquifex aeolicus holB* sequence was obtained by searching the *Aquifex aeolicus* genome with the sequence of the *T.th.* δ' (encoded by *holB*). The *Aquifex aeolicus holB* gene was amplified by PCR using the following primers: the upstream 39mer (5'-

GTGTGTCCATATGGAAAAAGTTTTTG_nAAACCTCCAG-3') (SEQ. ID. No. 161) contains an NdeI site (underlined); the downstream 35mer (5'-
GTGTGTGGATCCTTAATCCGCCTGAACGGCTAACG-3') (SEQ. ID. No. 162) contains a BamHI site (underlined). The PCR product was digested with NdeI and BamHI, purified, and ligated into the pET24 NdeI and BamHI site to produce pETAaholB.